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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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SYNNESTVEDT & LECHNER, LLP 2600 ARAMARK TOWER 1101 MARKET STREET PHILADELPHIA, PA 191072950				
			EXAMINER GROSS, CHRISTOPHER M	
			ART UNIT 1639	PAPER NUMBER

DATE MAILED: 07/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.		Applicant(s)	
	10/671,341		BAUM, STEPHEN A.	
	Examiner		Art Unit	
	Christopher M. Gross		1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 October 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 46,47 and 49-65 is/are pending in the application.
- 4a) Of the above claim(s) 59 and 63-65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 46-47,49-58,60-62 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The Office Action mailed 1/19/2006 is hereby vacated because claims 52, 53 and 60-62 were not addressed in the final rejection mailed 1/19/2006.

The Examiner on the instant case has changed. See contact information below.

Claims 46-47, 49-65 are pending. Claim 48 has been canceled by the amendment filed on 10/21/05. Claims 59 and 63-65 are withdrawn from consideration. Claims 46-47, 49-58 and 60-62 are examined herein.

Election/Restrictions

1. Applicant's election without traverse of (a): "a rack having a plurality of rods sized to be inserted through an aperture formed in each support and a mechanism to prevent the supports from coming off the rack " for the support transfer device of claims 52 and 53 and "polypropylene spheres" for the composition and shape set forth in claims 57 and 58 in the reply filed on 1/10/2005 is acknowledged.
2. Claim 59 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Furthermore, in the interest of compact prosecution, claims 63-65 are withdrawn because it is noted that claims 63-65 do not read on the elected species of support transfer device, mentioned above, since these claims address "the transfer block" which refers to the support transfer device species (c) of claims 52 and 53, rather than the elected species. Election was made **without** traverse in the reply filed on 1/10/2005.

Oath/Declaration

3. The objection to the oath or declaration set forth in the previous office action mailed on 4/21/05 has been withdrawn in view of the ADS, and applicant's response.

Specification

4. The amendment to the specification to update the parent application data has been considered and entered 10/21/2005.

Priority

5. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 120 is acknowledged: this application is a DIV of 09/082,038 05/20/1998 (now PAT 6,872,535).

Withdrawn Claim Rejections

6. The new matter rejection of claims 57 and 60 has been withdrawn in view of the amendment to the claims filed on 10/21/05.
7. The written description rejection of claims 46-51 and 54-58 set forth in the previous office action has been withdrawn in view of the amendment and response.
8. The rejection of claims 46-58 and 60-62 under 35 U.S.C. 112, as being indefinite has been withdrawn in view of the amendment and response filed on 10/21/05.

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9. The rejection of claims 46-47, 50, 51 and 55-58 under 35 U.S.C. 102(e) as being anticipated by Campbell et al. US Pat. No. 6,083,682 (7/00: filed 12/97) has been withdrawn in view of the amendment filed on 10/21/05.

10. The rejection of claims 46-47, 49-51 and 54-58 under 35 U.S.C. 103(a) as being unpatentable over Campbell US Pat. No. 6,083,682 (7/00: filed 12/97) and Hudson US Pat. No. 5,585,275 (12/96) has been withdrawn in view of the amendment filed on 10/21/05.

Maintained Claim Rejections

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. The obviousness-type double patenting rejection of claims 46-47, 49, 51 and 54-58 over claims 1-12 of U.S. Patent No. 6,541,211, has been maintained for the reasons of record. The rejection is copied below for the convenience of the reader.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent claims teach stacked (e.g. in a Z direction) a plurality of 2-D frames (e.g. a plurality of planes) forming a 3D array and the placement of supports with building blocks therein (e.g. functionalized supports with attached R1 groups) for parallel syntheses of combinatorial libraries. The patent claims teach spherical polypropylene supports (e.g. lanterns. Gears) within the scope of the present invention. Additionally, the supports are removable while retaining spacial addresses (e.g. see patent claim 3). Devices for achieving the claimed placement and removal of solid supports while retaining spacial addresses are described, said devices being within the scope of the presently claimed invention.
See.e.g. fig. 4-7.

Response to Arguments

Applicant's arguments filed on 10/21/05, regarding the obviousness-type double patenting rejection of claims over US patent 6,541,211 B1, have been fully considered but they are not persuasive.

Applicants argue that the present claims recite a "functionalizing a plurality of solid supports"; and the reference claims do not recite the step of functionalizing the solid supports.

Applicant's arguments are not persuasive since the reference claims recite a method of synthesizing combinatorial libraries on solid supports; and the solid supports are lanterns. The Examiner concedes that the claims do not recite the step of 'functionalizing,' however, the reference in the specification discloses that said 'lantern' is made of polypropylene with polystyrene surface; and the polystyrene surface is *functionalized* to react with reagents used in synthesizing the compound libraries (i.e., see column 15). Thus, the solid supports (lanterns) used in the reference claimed methods are 'functionalized' such that the reagents further would react with the surface, and therein functionalize the lantern.

Thus, the obviousness-type double patenting rejection of record has been maintained.

12. The rejection of claims 46-47, 49-51 and 54-58 under 35 U.S.C. 103(a) as being unpatentable over **Campbell** US Pat. No. 6,083,682 (7/00: filed 12/97) in view of any of **Nova et al.** US Pat. No. 5,961,923 (10/99: filed 9/96 or earlier), **Moran et al.** WO 97/35198 (9/97: filed 3/96) or **Lebl et al.** US Pat. No 6,045,755 (4/00: filed 3/97), each

taken separately has been maintained for the reasons of record. The rejection is copied below for the convenience of the reader.

The presently claimed invention is directed to a method comprising:

- a) functionalizing a plurality of supports;
- b) placing the supports in a 3D array; and
- c) performing parallel syntheses of a library of molecules in the 3D array of supports with 3D diversity. See claim 46.

Claim 48 further claims a "support transfer device" for placing the supports in the 3D array. Claim 49 further claims a "support transfer device" for "removing the plurality of supports. Claim 54 further requires that the "support transfer device" remove the supports one Z plane at time.

Campbell et al. disclose a system for parallel syntheses of a combinatorial library comprising a 3D array of aligned solid phase supports with a channel in fluid communication which are comprised of stackable middle plates (e.g. 2-D frames) with a plurality of reaction zones (e.g. functionalized /derivatized solid supports graft copolymers of poly/ethylene or propylene etc: see col. 12:) attached to said frames (e.g. see bottom of col. 2; col. 6; bottom of col. 19-col. 20, which includes sheets and resin beads). See e.g. see col. Col. 4; figures 1-15 and patent claims. The solid supports (e.g. sheets or resin beads) abut each other and are adapted to being coupled together (e.g. indeed may be stacked). The supports (e.g. polypropylene: including membranes or sheets/beads or spheres : see col. 12-13) are functionalized with the further attachment of one or more monomers before placement of the support in the apparatus (e.g. see bottom of col. 4; col. 9, especially lines 45-55: " solid support which is preferably prederivatized ... " ; col. 12; col 17, especially lines 33-41: "The supports 36 are preferably each provided with an initial building block (e.g. "R1") derivatized thereon before they are placed in the reaction vessels"). The reference teaches that the derivatized supports in the 3D array may possess columns having uniquely R1 (initial monomer) members. See e.g. col. 4, especially lines 28-67, especially lines 54-65). Additionally, the Campbell reference disclosed reaction zones in 3D (e.g. length/width height) form a column (e.g. see col. 3, lines 1-15) of reaction zones containing a single support (or multiple supports) within each cylindrical member (38) (e.g. a well). It is noted that the wells contain reaction zones which are in the shape of a trough or are cylindrical (e.g. see figures e.g. 4, 5, 7

and 9) and the plurality of 3D stacked solid supports are contained within a plurality of reactors which are sized to allow complete immersion in a reagent (e.g. see fig. 4: reaction vessel 30; solid support 36; and col. 10). Following syntheses, the synthesized compounds are cleaved from the solid supports (e.g. see col. 18, especially lines 24-45).

The Campbell method differs from the presently claimed invention by failing to explicitly teach:

- a. "A support transfer device" for placing the supports in the 3D array (CIm 48);
- b. "A support transfer device" for removing the plurality of supports (CIm 49); and.
- c. That the "support transfer device" removing the supports one Z plane at a time (CIm 54).

Support (e.g. polymeric i.e. polypropylene; of different shapes i.e. beads etc.) transfer devices (e.g. including automated) for placing and/or removal of the supports from in parallel synthetic array system (e.g. while retaining spatial addresses) for achieving high throughput syntheses/screening were known in the art.

Nova et al. disclose devices (e.g. including funnels: i.e. see figures, especially figures 6-9; 11-13) for removal/placement of solid supports (e.g. col. 11-12: MICROBALLS; MICROTUBES; col. 24; col. 44 especially tagged: ie. Col. 61-62) into/from a parallel syntheses apparatus.

Moran et al. disclose a method of performing parallel spatially addressable syntheses in which the supports (e.g. polyethylene crowns) are arranged (e.g. placed) and removed (e.g. redistributed) in a manner between a series of arrays in order to maintain the physical location (e.g. spatial address) via carrier devices, which are automatable (see pages 9-17 ; examples; claims).

Lebl et al. teach an integrated robotic apparatus for parallel spatially addressable high throughput 2D/3D (e.g. stacked support) syntheses. Various automated devices (e.g. storage vessels, pumps and multiple tips) for dispensing solid supports onto the synthetic 2D/3D apparatus and devices (e.g. gripper tools) for removing solid supports from the synthetic apparatus are taught. See figures, especially figures, especially figures 1-9, 11; col. 5-7; col. 10-37; examples; patent claims

One of ordinary skill in the art at the time of applicant's invention would have been motivated to utilize conventionally available Nova/Moran/Lebl support transfer devices in the Campbell et al. reference method since these conventional devices address parallel syntheses as in the Campbell reference and would further lead to improved high-throughput syntheses/screening and/or ease of support transfer, especially when automated.

Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to utilize the Nova/Moran/Lebl support transfer devices in the Campbell reference method and arrive at the presently claimed invention.

Response to Arguments

Applicant's arguments filed on 10/21/05, regarding the rejection of claims over Campbell, Nova et al, Moran et al or Lebl et al, have been fully considered but they are not persuasive.

Applicants traverse the rejection. Applicants argue that Nova et al discloses placement of solid support using an apparatus that places or removes microballs or microtubes one at a time. Nova et al do not disclose that the placement of solid supports is performed with a support transfer device that transfers a plurality of supports at a time. Applicant's arguments have been considered and are not persuasive.

In response to applicant's arguments against the references individually (Nova et al, and Moran et al, and Lebl et al), one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case the rejection was based on combined teachings of Campbell, Nova et al, Moran et al or Lebl et al. Additionally, it is noted that the features upon which applicant relies (i.e., 'the placement of solid supports is performed with a support transfer device that **transfers a plurality of supports at a time**') are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicant's argument that there is no suggestion to combine the references, the Examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the references provide the advantages of automation in combinatorial synthesis (Lebl/Nova/Moran), and teach the apparatus (Campbell) used in the combinatorial synthesis.

Nova et al in column 6, lines 9-19 teach that high throughput screening has assumed importance in the pharmaceutical industry and the exploitation of the diversity afforded by combinatorial chemistry requires methods for rapidly screening compounds. Lebl in column 3, lines 17-19 teach that the currently available robotics are slow and limit the promise of combinatorial chemistry. On p4, lines 32-33, Moran et al state the need for geometric amplification in the number library members synthesized, therein placing even greater demand on high throughput techniques.

In response to applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a

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reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant's arguments that there is no teaching in Nova, Moran, or Lebl either individually or any combination thereof, which would yield a transfer device that transfers a plurality of solid phase supports. Applicants arguments have been considered and are not persuasive, because Nova et al disclose devices for removal and replacement of solid supports; Moran et al disclose devices used in combinatorial synthesis; and Lebl et al disclose robotic apparatus for parallel synthesis; and Campbell et al teach a system for parallel syntheses of a combinatorial library comprising a 3D array of aligned solid phase supports. Thus, it would have been obvious to one skilled in the art to use the devices taught by Nova et al, Moran et al or Lebl et al with the method taught by Campbell et al. A person skilled in the art would have been motivated to use the combinatorial library synthesis apparatus taught by the references in concert with the combinatorial methods taught by Campbell et al for the ease of support transfer and/or improved high-throughput syntheses and screening achieved by automation.

New Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 46-47, 49-51, 52-58, 60-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Campbell** US Pat. No. 6,083,682 (7/00: filed 12/97) in view of **Moran et al.** WO 97/35198 (9/97: filed 3/96) as evidenced by Valerio et al (1993 Int. J. Peptide Protein Res. 42:1-9). Valerio et al provides evidence pertaining to claims 52-53, 60-62. This new ground of rejection is necessitated by amended claim 46, now drawn to a support transfer device wherein the support transfer device transfers a plurality of supports.

Claims 52 and 53 add the limitation of a transfer device consisting essentially of a rack having a plurality of rods sized to be inserted through an aperture formed in each support and a mechanism to prevent the supports from coming off the rack. Claim 60 adds the limitation that the rack comprise a device to keep the supports immersed in liquid. Claim 61 adds the limitation that the mechanism for preventing the removal of the supports from the rack comprises an end cap attached to the end of at least one rod. Claim 62 adds the limitation that the device to keep the supports immersed liquid comprises an obstruction device that limits the movement of the supports on the rods.

Campbell is relied on as per the previous maintained rejections.

Campbell does not teach a transfer device bearing a plurality of rods sized to be inserted through an aperture formed in each support and a mechanism to prevent the supports from coming off the rack, however.

Moran et al teach, throughout the document and especially example 1, Chiron Mimotope synthetic support crowns and crown holders (carriers) arranged in a 8 x 8 array (rack), which are used as a "transfer device" to move the synthetic crowns into

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various wash solvents, etc. As evidenced by Valerio et al, in figure 1 the crown carriers of Moran et al are rods comprising an end cap, onto which the crown synthetic supports are snapped on. The snapping action prevents the crown(s) from coming off the rack, keeps the crown(s) immersed in liquid and limits the crown movement. The array of crown holders of Moran et al is taken as "a plurality of rods sized to be inserted through an aperture formed in each support and a mechanism to prevent the supports from coming off the rack" (elected species of claims 52 and 53) as well as meets all the limitations set forth in claims 60-62.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to use synthetic crown and crown carrier system of Moran et al with the cubic apparatus for the parallel synthesis of a combinatorial collection of compounds of Cambell et al.

One of ordinary skill in the art would have been motivated to the use crowns and crown carrier of Moran et al with the cubic apparatus for the parallel synthesis of a combinatorial collection of compounds of Campbell et al. because the crown system provides more material (micromolar amounts) than the small synthetic beads of Campbell, which is desirable according to Moran on p4, lines 36 and 37.

One of ordinary skill could do so with a reasonable expectation of success since crown methodology is well established in the art.

Conclusion

Claims 46-47, 49-58 and 60-62 are not allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Gross whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher M Gross
Examiner
Art Unit 1639

cg

PETER PARAS, JR.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

A handwritten signature in black ink, appearing to read "Pete Paras", written in a cursive style.